

FILE 'USPAT' ENTERED AT 08:45:23 ON 26 MAY 94

```
* * * * *
*           W E L C O M E   T O   T H E           *
*           U . S .   P A T E N T   T E X T   F I L E   *
* * * * *
```

=> e jutila/in

```
E1          1      JUTERBOCK, KARSTEN/IN
E2          1      JUTIER, PIERRE/IN
E3          0 --> JUTILA/IN
E4          1      JUTILA, PENTTI K/IN
E5          1      JUTILA, RAYMOND E/IN
E6          2      JUTILA, RAYMOND EINO/IN
E7          1      JUTKEVICH, VALERY I/IN
E8          1      JUTKEVICH, VALERY IVANOVICH/IN
E9          1      JUTO, YASURO/IN
E10         1      JUTRAS, GILLES/IN
E11         1      JUTRAS, MARIO/IN
E12         1      JUTRAS, MARTIAL/IN
```

=> s lam(w)1 or lecam(w)1 or l(w)selectin

```
        605 LAM
        1802011 1
                                11 LAM(W)1
        6 LECAM
        1802011 1
                                1 LECAM(W)1
        396493 L
        24 SELECTIN
        1 L(W)SELECTIN
L1          11 LAM(W)1 OR LECAM(W)1 OR L(W)SELECTIN
```

=> s elam or elam(w)1 or e(w)selectin

```
                                85 ELAM
        85 ELAM
        1802011 1
        18 ELAM(W)1
        1034832 E
        24 SELECTIN
        2 E(W)SELECTIN
L2          85 ELAM OR ELAM(W)1 OR E(W)SELECTIN
```

=> s l1 and l2

```
L3          5 L1 AND L2
```

=> d l3 1-5

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand;  
Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1  
[IMAGE  
AVAILABLE]

2. 5,252,602, Oct. 12, 1993, Effects of misoprostol on allergic responses; Rafeul Alam, et al., 514/530, 573, 826 [IMAGE AVAILABLE]

3. 5,227,369, Jul. 13, 1993, Compositions and methods for inhibiting leukocyte adhesion to CNS myelin; Steven Rosen, et al., 514/23, 2, 3, 4, 8, 885, 903 [IMAGE AVAILABLE]

4. 5,198,424, Mar. 30, 1993, Functionally active selectin-derived peptides; Rodger P. McEver, 514/13; 424/1.37, 1.69; 427/2; 514/12, 14, 15, 16; 530/324, 325, 326, 327; 623/11 [IMAGE AVAILABLE]

5. 5,151,360, Sep. 29, 1992, Effect of N,N,N-trimethylsphingosine on protein kinase-C activity, melanoma cell growth in vitro, metastatic potential in vivo and human platelet aggregation; Kazuko Handa, et al., 435/240.2, 240.1 [IMAGE AVAILABLE]

```
=> s l3 and common(w)epitope
      472958 COMMON
      1273 EPITOPE
      62 COMMON(W) EPITOPE
L4      0 L3 AND COMMON(W) EPITOPE
```

```
=> s l3 and scr
      10597 SCR
L5      1 L3 AND SCR
```

```
=> d l5 1
```

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand; Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1 [IMAGE AVAILABLE]

```
=>
```

FILE 'USPAT' ENTERED AT 08:45:23 ON 26 MAY 94

```
* * * * *
*           W E L C O M E   T O   T H E           *
*           U . S .   P A T E N T   T E X T   F I L E   *
* * * * *
```

=> e jutila/in

```
E1          1      JUTERBOCK, KARSTEN/IN
E2          1      JUTIER, PIERRE/IN
E3          0 --> JUTILA/IN
E4          1      JUTILA, PENTTI K/IN
E5          1      JUTILA, RAYMOND E/IN
E6          2      JUTILA, RAYMOND EINO/IN
E7          1      JUTKEVICH, VALERY I/IN
E8          1      JUTKEVICH, VALERY IVANOVICH/IN
E9          1      JUTO, YASURO/IN
E10         1      JUTRAS, GILLES/IN
E11         1      JUTRAS, MARIO/IN
E12         1      JUTRAS, MARTIAL/IN
```

=> s lam(w)1 or lecam(w)1 or l(w)selectin

```
        605 LAM
        1802011 1
                                11 LAM(W)1
        6 LECAM
        1802011 1
                                1 LECAM(W)1
        396493 L
        24 SELECTIN
        1 L(W)SELECTIN
L1          11 LAM(W)1 OR LECAM(W)1 OR L(W)SELECTIN
```

=> s elam or elam(w)1 or e(w)selectin

```
                                85 ELAM
        85 ELAM
        1802011 1
        18 ELAM(W)1
        1034832 E
        24 SELECTIN
        2 E(W)SELECTIN
L2          85 ELAM OR ELAM(W)1 OR E(W)SELECTIN
```

=> s l1 and l2

L3 5 L1 AND L2

=> d l3 1-5

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand;  
Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1  
[IMAGE  
AVAILABLE]

2. 5,252,602, Oct. 12, 1993, Effects of misoprostol on allergic responses; Rafeul Alam, et al., 514/530, 573, 826 [IMAGE AVAILABLE]

3. 5,227,369, Jul. 13, 1993, Compositions and methods for inhibiting leukocyte adhesion to CNS myelin; Steven Rosen, et al., 514/23, 2, 3, 4, 8, 885, 903 [IMAGE AVAILABLE]

4. 5,198,424, Mar. 30, 1993, Functionally active selectin-derived peptides; Rodger P. McEver, 514/13; 424/1.37, 1.69; 427/2; 514/12, 14, 15, 16; 530/324, 325, 326, 327; 623/11 [IMAGE AVAILABLE]

5. 5,151,360, Sep. 29, 1992, Effect of N,N,N-trimethylsphingosine on protein kinase-C activity, melanoma cell growth in vitro, metastatic potential in vivo and human platelet aggregation; Kazuko Handa, et al., 435/240.2, 240.1 [IMAGE AVAILABLE]

```
=> s l3 and common(w)epitope
      472958 COMMON
      1273 EPITOPE
      62 COMMON(W) EPITOPE
L4      0 L3 AND COMMON(W) EPITOPE
```

```
=> s l3 and scr
      10597 SCR
L5      1 L3 AND SCR
```

```
=> d l5 1
```

1. 5,304,640, Apr. 19, 1994, DNA sequence encoding a selectin ligand; Laurence A. Lasky, et al., 536/23.5; 435/69.1, 172.3, 240.2, 320.1 [IMAGE AVAILABLE]

```
=>
```

19863 EL  
4345 246  
S1 4 EL(W) 246  
?^Q  
...completed examining records  
S2 2 RD S1 (unique items)  
?^Q

2/7/1 (Item 1 from file: 55)  
DIALOG(R) File 55: BIOSIS PREVIEWS(R)  
(c) 1994 BIOSIS. All rts. reserv.

9535279 BIOSIS Number: 94040279

CHARACTERIZATION OF A FUNCTIONALLY IMPORTANT AND EVOLUTIONARILY  
WELL-CONSERVED EPITOPE MAPPED TO THE SHORT CONSENSUS REPEATS OF E  
SELECTIN  
AND L SELECTIN

JUTILA M A; WATTS G; WALCHECK B; KANSAS G S  
VETERINARY MOLECULAR BIOLOGY, MONTANA STATE UNIVERSITY, BOZEMAN,  
MT  
59717.

J EXP MED 175 (6). 1992. 1565-1573. CODEN: JEMEA  
Full Journal Title: Journal of Experimental Medicine  
Language: ENGLISH

Selectins represent a new family of adhesion molecules,  
expressed by  
leukocytes and endothelial cells, that are involved in the  
regulation of  
leukocyte traffic. Here we have characterized a new monoclonal  
antibody  
(mAb) (EL-246) that recognizes both human leukocyte L-selectin  
(previously  
called LAM-1, LECAM-1, or gp90MEL-14) and endothelial cell  
E-selectin  
(previously called ELAM-1). EL-246 recognized a 110-kD protein  
expressed on  
cells transfected with E-selectin cDNA and stained many  
postcapillary  
venules in inflamed human tonsil. EL-246 also stained human  
peripheral  
blood leukocytes and showed identity with anti-L-selectin mAb in  
two-color  
flow cytometric analysis. The expression of the leukocyte EL-246  
antigen  
was regulated in the same manner as L-selectin and EL-246  
recognized  
anti-L-selectin mAb affinity-purified antigen in SDA/PAGE  
Western blot  
analysis. Further, L-selectin cDNA transfectants were specifically  
stained  
by EL-246. EL-246 blocked >95% of lymphocyte adhesion to  
peripheral lymph  
node high endothelial venules and >90% of neutrophil adhesion to

E-selectin transfectants. In addition to the EL-246 epitope being expressed on two different human selectins, it was detected on L-selectin from a variety of different animals. Interestingly domain mapping studies localized the EL-246 epitope to the short consensus repeat (SCR) domains of L-selectin. EL-246 is the first mAb that recognizes two different selectins and potentially defines a functional epitope encoded by the SCR domains. Inhibitors of selectin function targeted to this region would be expected to have the added advantage of simultaneously blocking the activity of two distinct of adhesion protein involved in inflammation.

2/7/2 (Item 1 from file: 72)  
DIALOG(R)File 72:EMBASE  
(c) 1994 Elsevier Science B.V. All rts. reserv.

9171016 EMBASE No: 94118088

Survival in lung reperfusion injury is improved by an antibody that binds and inhibits L- and E-selectin  
Steinberg J.B.; Mao H.-Z.; Niles S.D.; Jutila M.A.; Kapelanski D.P.

Division of Cardiothoracic Surgery, UCSD Medical Center, 225 Dickinson

St., San Diego, CA 92103-8892 USA

J. HEART LUNG TRANSPLANT. (USA) , 1994, 13/2 (306-318) CODEN: JHLTE

ISSN: 1053-2498

LANGUAGES: English SUMMARY LANGUAGES: English

The selectins are a three-member family of leukocyte, platelet, and endothelial cell adhesion proteins that mediate leukocyte traffic into normal and inflamed tissues. P-selectin is expressed by endothelial cells and platelets, E-selectin by endothelial cells, and L-selectin by circulating leukocytes. To determine if selectin-mediated leukocyte adhesion influences the development of lung reperfusion injury, we studied hemodynamics and respiratory and inert gas exchange in sheep subjected to 3-hour in situ left lung ischemia followed by 6-hour left lung reperfusion with the right lung excluded. Ten minutes before reperfusion, eight

animals received EL-246 (1 mg/kg intravenously), a novel antihuman selectin antibody that recognizes and blocks both L- and E-selectin and cross-reacts in sheep. Eight control animals with ischemia received no treatment, whereas three received an isotype-matched antihuman L-selectin antibody that does not cross-react in sheep (DREG-56, 1 mg/kg intravenously). Eight sham control sheep underwent an identical operative procedure but were never subjected to ischemia. Volume-cycled, pressure-limited (20 cm H<sub>2</sub>O) mechanical ventilation was consistent in all animals throughout the experiment. Six-hour survival in EL-246 recipients (100%) was significantly higher than in either ischemic control sheep (37.5%) or DREG-56 recipients (33.3%), but gravimetric lung water was equivalent in EL-246 recipients (5.9 plus or minus 1.7 ml/kg), ischemic control sheep (8.3 plus or minus 3.0 ml/kg), and DREG-56 recipients (9.1 plus or minus 2.6 ml/kg). Although inert gas shunt at one-half hour of reperfusion was no different when contrasted in EL-246 recipients (15% plus or minus 8%), ischemic control sheep (30% plus or minus 25%), and DREG-56 recipients (35% plus or minus 21%), shunts in EL-246 recipients resolved (4% plus or minus 4%) within the 6-hour study period and were associated with a concomitant improvement in respiratory gas exchange. Peripheral blood neutrophil counts increased after both EL-246 and DREG-56 administration, suggesting that the beneficial effect of EL-246 was not incurred by leukocyte depletion. We conclude that mechanisms other than activated neutrophils may account for the initial deterioration of respiratory gas exchange in lung reperfusion injury and inhibition of selectin function improves survival by preventing leukocyte-mediated amplification of this early process.

?